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AN 2004444159 EMBASE
TI Involvement of inducible costimulator in the exaggerated memory B cell and plasma cell generation in systemic lupus erythematosus.
AU Hutloff A.; Buchner K.; Reiter K.; Baelde H.J.; Odendahl M.; Jacobi A.; Dorner T.; Kroczek R.A.
CS Dr. R.A. Kroczek, Molecular Immunology, Robert Koch Institute, Nordufer 20, D-13353 Berlin, Germany. kroczek@rki.de
SO Arthritis and Rheumatism, (2004) Vol. 50, No. 10, pp. 3211-3220. .
Refs: 42
ISSN: 0004-3591 CODEN: ARHEAW
CY United States
DT Journal; Article
FS 005 General Pathology and Pathological Anatomy
026 Immunology, Serology and Transplantation
028 Urology and Nephrology
031 Arthritis and Rheumatism
LA English
SL English
ED Entered STN: 12 Nov 2004
Last Updated on STN: 12 Nov 2004
AB Objective. In systemic lupus erythematosus (SLE), the increased generation of memory B cells and plasma cells leads to autoimmune hypergammaglobulinemia and destructive immunoglobulin deposits in the kidneys. We undertook this study to determine the biologic mechanism driving this overactivation of the B cell compartment, which is the central issue in SLE. Methods. We used flow cytometry to analyze expression of the T cell-specific inducible costimulator (ICOS) and its ligand (ICOS-L) on B cells obtained from the peripheral blood of SLE patients. We correlated ICOS-L expression with the differentiation status of the B cells using a large panel of surface antigens. In addition, SLE kidneys were analyzed by immunohistology. Results. We found an increased expression of ICOS on CD4+ as well as CD8+ T cells in SLE. At the same time, we documented a down-regulation of ICOS-L on a high proportion of peripheral blood memory B cells. Based on in vitro experiments, we inferred that this ICOS-L down-regulation on B cells was a signature of recent interaction with ICOS+ T cells in vivo. In the kidneys of SLE patients, we found clusters of B cells and plasma cells in close contact with ICOS+ T cells. Conclusion. Detailed analysis of B cells with down-regulated ICOS-L suggests that ICOS is one of the forces driving the formation of memory B cells and plasma cells in SLE. Furthermore, our identification of plasma cells in areas of T cell-B cell interaction in kidneys suggests that components of a T cell-driven B cell activation process may take place in peripheral tissues in SLE.

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L4 998 S ICOS (S)("INDUCIBLE COSTIMULATOR" OR "INDUCIBLE CO-STIMULATOR
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